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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/709,774	11/08/2000	Alessandro Sette	18623006240	3936

20350 7590 07/11/2005

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EXAMINER	
VANDERVEGT, FRANCOIS P	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 07/11/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/709,774	SETTE ET AL.	
	Examiner	Art Unit	
	F. Pierre VanderVegt	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-23,25 and 66-72* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-23,25 and 66-72* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

8.00

DETAILED ACTION

This application is a continuation-in-part of U.S. Application Serial Number 08/305,871, which is a continuation-in-part of U.S. Application Serial Number 08/121,101, and is a continuation-in-part of U.S. Application Serial Number 08/788,822, which claims the benefit of the filing date of provisional applications 60/082,250, 60/101,580 and 60/010,510.

Claims 1-17, 24 and 26-65 have been canceled.

New claims 66-72 have been added.

Claims 18-23, 25 and 66-72 are currently pending and are the subject of examination in the present Office Action.

1. In view of Applicant's amendment and response filed April 1, 2005, no outstanding grounds of rejection are maintained.

The following represent NEW GROUNDS of rejection and necessitate that the instant Office Action be made NON-FINAL.

Applicant's arguments with respect to claims 18 and 66 have been considered but are moot in view of the new ground(s) of rejection.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

2. Claims 18-23 and 25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well-established utility.

Base claim 18 recites a polynucleotide encoding a fusion protein comprising at least one pan DR binding peptide comprising SEQ ID NO: 22 and at least one CTL-inducing peptide. The disclosed utility of the claimed invention is to provide peptides for inducing or enhancing an immune response (page 3, line 29 through page 4, line 15 for example). It is well established in the art that HLA class II molecules present peptide antigens to helper (CD4+) T lymphocytes, which specifically recognize the peptide antigen in context of a specific HLA class II molecule. It is also well established that CD8+ cytotoxic T lymphocytes (CTL) recognize specific immunogenic peptides in context of HLA class I molecules. The presently claimed invention consists of a nucleic acid encoding a fusion protein comprising a CTL-stimulating peptide fused to an HLA-DR binding peptide. HLA-DR is a class II molecule. Accordingly,

CTL-stimulating peptides bound to the pan-DR binding peptide that is, in turn, bound to HLA-DR cannot be properly presented to CTL. Furthermore, the fusion peptide cannot be processed to separate the CTL peptide from the pan-DR binding peptide and separately present it to CTL in the context of HLA class I. It is well known in the art that MHC class I molecules do not express antigenic peptides obtained via the exogenous pathway, a function exclusive to MHC class II. MHC class I molecules can only express endogenous antigens. See, for example, the illustration from the immunology textbook "Kuby Immunology" (Kuby Immunology, 2000; U on form PTO-892). Additionally, the entire pan-DR binding peptide:CTL peptide construct cannot be presented as an intact peptide in the context of HLA class I because the binding pockets of MHC class I molecules are closed and cannot accommodate peptides of greater than 12 amino acid residues in length.

Accordingly, the claimed invention lacks a well-established utility because CTL peptides are known in the art not to be presented to CTL by HLA class II. The claimed invention lacks a credible asserted utility because one skilled in the art would not find it credible that the CTL peptide could remain attached to the pan-DR binding peptide and be presented in the context of HLA class I or HLA class II to a CTL in order to stimulate the CTL, nor can the CTL peptide be processed according to the exogenous pathway and associated with HLA class I. Applicant is directed to the Utility Examination Guidelines, Federal Register, Vol. 66, No. 4, pages 1092-1099, Friday January 5, 2001.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

3. Claims 18-23 and 25 are rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a credible asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention.

4. Claims 66-72 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a nucleotide encoding a fusion protein comprising a pan-DR binding peptide and a T-helper epitope that is presentable by HLA-DR, does not reasonably provide enablement for the full scope of nucleotide encoding a fusion protein comprising a pan-DR binding peptide and non-DR presentable T-

helper epitope. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use the invention commensurate in scope with these claims.

Base claim 66 recites a polynucleotide encoding a fusion protein comprising at least one pan DR binding peptide comprising SEQ ID NO: 22 and at least one T helper peptide. The disclosed utility of the claimed invention is to provide peptides for inducing or enhancing an immune response (page 3, line 29 through page 4, line 15 for example).

In order for a compound to be enabled for the scope of a claim, the compound must be usable for the processes disclosed in the specification.

It is well established in the art that CD4+ T cells specifically recognize presenting peptides in the context of a particular MHC class II heterodimer (see, for example, pages 291-293 of Germain *in* Fundamental Immunology, Fourth Edition; U on form PTO-892). It is further well known that HLA class II heterodimers specifically bind presenting peptides based upon the position of particular anchor residues within the sequence of the presenting peptide (pages 298, 300-301 and 303 for example). The present invention provides a peptide, SEQ ID NO: 22, that is capable of binding a plurality of HLA-DR haplotypes. The peptide of SEQ ID NO: 22 has not, however, been demonstrated to be able to bind other HLA class II haplotypes. Accordingly, use of the present invention requires the binding of the fusion protein to an HLA class II molecule that is of a DR haplotype and the resultant complex can only present to a helper T cell that recognizes antigenic peptides in the context of HLA-DR.

The instant claims, however, are not limited to constructs comprising a T helper peptide that is specifically presentable by the HLA-DR class II molecule to which it is attached. Based upon the lack of guidance in the specification, the artisan would not be able to determine whether the T helper peptide of such a construct would be able identified as a peptide recognized by a T cell receptor unless that T helper peptide is normally presented by an HLA-DR class II molecule because the T cell would not be able to recognize a T helper peptide normally presented in the context of a non-HLA-DR class II molecule.

The artisan would not be able to predict that the full scope of fusion proteins encoded by the invention would be able to suppress an immune response or induce a desired immune response, because any peptide presented in the context of a non-HLA-DR class II molecule of the complex would not be properly associated with the class II HLA-DR molecule to which it is bound.

Accordingly, only polynucleotides encoding a pan-DR binding peptide fused to a T helper peptide presentable by HLA-DR are adequately enabled by the instant specification.

Conclusion

5. No claim is allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to F. Pierre VanderVegt whose telephone number is (571) 272-0852. The examiner can normally be reached on M-Th 6:30-4:00 and Alternate Fridays 6:30-3:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (571) 272-0841. The fax phone number for the organization where this application or proceeding is assigned is (571) 273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

F. Pierre VanderVegt, Ph.D.
Patent Examiner
July 7, 2005

David A Saunders

DAVID SAUNDERS
PRIMARY EXAMINER
ART UNIT ~~182~~ 1644